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ALEXANDRIA, VA 22314				
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YEAGER, RAYMOND P				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/590,451

Applicant(s)

JOKINEN ET AL.

Examiner

Raymond P. Yeager

Art Unit

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 February 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 20-29, 31-35 and 38-50 is/are pending in the application.
- 4a) Of the above claim(s) 22-26, 28, 31-32, 36-38, 40, 42-45, and 48 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21, 27, 33-35, 39 and 46 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-940)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Applicant's arguments filed 02/17/2010 have been fully considered. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

- Claims 20 to 29, 31 to 35 and 38 to 50 are pending;
- Claims 20 to 29 and 31 to 35 have been amended;
- Claims 1 to 19, 30, and 36 to 37 have been cancelled;
- Claims 22 to 26, 28, 31 to 32, 36 to 38, 40, 42 to 45, and 48 have been withdrawn;
- Claims 38 to 50 are new;
- Claims 21, 27, 29, 33 to 35, 39, and 46 to 47 are under consideration.

Election/Restriction

For convenience the applicant's species election within group II is recited here: The species embodiment of the sol-gel as elected in the applicant's 02/26/2009 response to the restriction requirement: sol-gel **derived SiO₂ monolith containing a biologically active agent.**

REJECTION/OBJECTION STATUS

Rejections/Objections Withdrawn

• *Objections - Abstract*

○ Applicant's arguments have been fully considered and are persuasive. The objection to the abstract has been withdrawn due to applicant's amendment.

• *Objections - Claims*

○ Applicant's arguments have been fully considered and are persuasive. The objection to claims 21, 27, 29, and 33 to 35 has been withdrawn due to applicant's amendment.

○ Applicant's arguments have been fully considered and are persuasive. The objection to claims 21, 27, 29, and 33 to 35 has been withdrawn due to applicant's amendment.

Rejections/Objections Maintained

• Claim Rejections – 35 USC § 103

○ Applicant's arguments have been fully considered but they are not persuasive. The 35 USC § 103 rejection of claims 21, 27, 29, and 32 to 35 has been revised due to applicant's amendment and extended to new claims 39 and 46 to 47. Claims 21, 27, 29, 33 to 35, 39, and 46 to 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kortesuso, 2001 (Kortesuso Dissertation, University of Helsinki, 2001; as provided in the 02/26/2009 restriction requirement), as evidenced by Kortesuso et al, 2001a (*Journal of Controlled Release*, vol. 76:227-238).

Applicant has amended the claims to incorporate the process by which the product is made and further limited the dissolution rate to greater than or equal to 1, 2, or 4 weight percent per hour.

Rejection Reiterated

Applicant claims a bioresorbable sol-gel derived SiO₂ monolith comprising a biologically active agent (instant claims 21, 29, 39, and 47) with a dissolution rate greater than or equal to 2.0 or 4.0 weight percent per hour (instant claims 27, 34, and 46). Further the biologically active agent is claimed to be a peptide, protein, or cell (instant claim 33, 35).

Kortesuso, 2001 teaches a biodegradable (page 25, section 5.1.2) sol-gel derived SiO₂ monolith (page 10, section 2.3, paragraph 1 and page 25, section 5.1.2) which may incorporate cells (page 11, paragraph 1) (limitations in instant claims 21, 29, 33, 35, 39, and 47). Kortesuso, 2001 teaches the degradation over a 30-hour dissolution period was about 17 to 28 percent (page 25, section 5.1.1, paragraph 2) which is explicitly a dissolution rate of about 0.56 to 0.93 weight percent per hour and teaches degradation time of a monolith as low as 4 days (i.e. 100 percent dissolution in 96 hours or greater than 1 percent) or as high as 4 months (i.e. about 0.037 weight percent per

hour) (page 35, section 6.1.3) and *in vivo* may be about 10-fold slower than *in vitro* (i.e. about 0.056 weight percent) (page 35, section 6.1.3, paragraph 3) (limitations in instant claims 21, 29, 39, and 47). Degradation studies were performed at pH 7.4 and at 37° C in simulated body fluid (SBF) (page 22, section 4.4, paragraph 1) and as evidenced by Kortessuo et al, 2001a, SBF contains TRIS buffer (page 228, column 2, section 2.3, paragraph 1). Further, Kortessuo, 2001 teaches the pH and the water to alkoxide (or inorganic silicate) ratio affects the degradation rate (page 28, table 2) as does the surface area and geometry of the sol-gel derived SiO₂ (page 7, paragraph 3). Kortessuo, 2001 also teaches the porous structure alters the degradation rate of the sol-gel derived SiO₂ monolith (page 31, section 6.1) and larger gel monoliths degrade faster than smaller ones (page 35, section 6.1.3, paragraph 2). Kortessuo, 2001 teaches the water/alkoxide to alcohol ratio also affects the silica xerogel microstructure (page 12, section 2.3.1). Kortessuo, 2001 also teaches the degradation rate of the silica xerogel can be modified by varying the composition of starting materials and subsequently the structure of the silica gel matrix by varying the manufacturing method from casting to spray drying (page 35, section 6.1.3, paragraph 2). Kortessuo et al, 2001 does not explicitly exemplify the instantly claimed monoliths. The claims recite a dissolution rate of greater than or equal to 1, 2, or 4 weight percent per hour and Kortessuo, 2001 teaches lower pH and lower water to alkoxide ratio increases dissolution rate (page 26, paragraph 1). The U.S. Patent Office is not equipped with analytical instruments to test prior art compositions for the infinite number of ways that a subsequent applicant may present previously unmeasured characteristics. Applicant claims the sol-gel derived SiO₂ monolith by what it does not by what it is. In the instant application the claims recite a dissolution rate for the sol-gel derived SiO₂ monolith. When as here, the prior art appears to contain the exact same ingredients, the same method of combining the ingredients, and applicant's own disclosure supports the suitability of the prior art composition as the inventive composition component, the burden is properly shifted to applicant to show otherwise (limitations in instant claims 21, 27, 33, 34, and 46).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to make a sol-gel derived SiO₂ monolith as taught by

Kortesuo, 2001, with optimized surface area, geometry, pH and water/alkoxide ratio and with a higher (greater than or equal to 2 or 4 weight percent per hour) degradation rate as taught by Kortesuo, 2001. It further would have been obvious to one of ordinary skill in the art to use the sol-gel derived monoliths to deliver any biological agent of interest especially heat sensitive agents as taught by Kortesuo 2001 (abstract, page iii) including cells, peptides and proteins. One of ordinary skill in the art would have been motivated to do this because Kortesuo, 2001 teaches the sol-gel derived SiO_2 monoliths are a means to control the release rate of therapeutic substances (page 31, section 6.1, paragraph 1). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Applicant's Arguments

- Applicant argues neither the Kortesuo Dissertation nor Kortesuo et al, 2001a disclose or suggest and actually teaches away from a sol-gel derived SiO_2 in vitro dissolution rate of at least 1.0 wt-%/hour, or the combination of precursor ratios, pH and drying conditions necessary to achieve such an unexpectedly fast dissolving SiO_2 . The MPEP § 2141.02. VI. notes "the prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed...." [*In re Fulton*, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004). >See also MPEP § 2123.] Further, Kortesuo, 2001 teaches a monolith with a degradation time of 4 days or 96 hours (page 35, section 6.1.3., paragraph 2) which since degradation is 100 percent provides a degradation rate of greater than 1 weight percent per hour.
- Applicant argues Kortesuo, 2001 is merely an invitation to experiment, rather than guidance to one of ordinary skill in the art seeking to prepare a sol-gel derived SiO_2 having a very fast bioresorption rate and further argues Kortesuo, 2001 demonstrates

the prior art did not understand which factors are decisive to control the dissolution rate of bioresorbable sol-gel derived SiO₂. Applicant argues Kortesuo, 2001 provides only a very limited possibility of adjusting the dissolution rate of the silica gel of a monolith and applicant argues the parameters altering degradation rate independently. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., parameters which provide a specific degradation rate) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Further, the MPEP § 2141.02. VI. notes "the prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed...." [*In re Fulton*, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004). >See also MPEP § 2123.]. As discussed *supra*, Kortesuo, 2001 gives directions to optimize the parameters affecting degradation rate - Kortesuo, 2001 teaches lower pH and lower water to alkoxide ratio increases dissolution rate. Further, Kortesuo, 2001 teaches porous structure alters the degradation rate of the sol-gel derived SiO₂ monolith, larger gel monoliths degrade faster than smaller ones and the degradation rate of the silica xerogel can be modified by varying the composition of starting materials and subsequently the structure of the silica gel matrix. Also, the matrix may be modified by varying the manufacturing method from casting to spray drying. Thus the degradation rate is considered a result-effective variable per MPEP 2144.05.II.: "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. '[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.' [*In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)]." Regarding the degradation rate recited in instant claims; the degradation is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine

practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal pH, water to alkoxide ratio, and alcohol to alkoxide ratio needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention. Further, as noted in MPEP § 2144.05.II.B: "A particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. [*In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977)]". Note as discussed above, Kortesus, 2001 teaches a monolith with a degradation time of 4 days or 96 hours (page 35, section 6.1.3., paragraph 2) which since degradation is 100 percent provides a degradation rate of greater than 1 weight percent per hour and it would be obvious to optimize to a higher degradation rate in view of the discussion above.

- Applicant argues presents Viitala et al, 2005 (*Journal of Sol-Gel Science and Technology*, vol. 36:147-156; as provided by applicant in the 02/17/2010 response without an IDS) that provides factors which may be considered to have a greater effect on degradation rate. Viitala et al, 2005 also teaches that "simple adjustments of the sol component concentrations and sol aging result in both fast (days) and slow (weeks & months) dissolution" but regardless Viitala et al, 2005 is not considered prior art at the time the invention was made as the instant claims 21, 27, 29, 33 to 35, 39, and 46 to 47 are considered to have a priority date 02/27/2004. Further, Viitala et al, 2005 is not commensurate in scope with the claims as Viitala et al, 2005 compares specific alterations to water to alkoxide ratio, pH, hydrolysis time, drying time, types of drying, and ratios after dilution.

- Applicant argues Kortesus, 2001 fails to disclose or suggest a starting point for correlating the values necessary to produce a sol-gel derived SiO₂ having a specific dissolution rate, as demonstrated by the results listed in its Table 2. In stark contrast, the present application provides such a starting point. The application defines what changes result in slower dissolution rates, and defines the provisos related to having

these changes reduce the dissolution rate. Applicant's arguments are not commensurate in scope with the claims, in fact, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., specific starting point and parameters for specific dissolution rates) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

- **Double Patenting**

- Claims 21, 27, 29, 33 to 35, 39, and 46 to 47 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 24, 25, and 30 to 33 of copending Application No. 09/913,643 as evidenced by Kortesuo et al, 2001a. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are overlapping in scope.

Rejection Reiterated

The instant application claims a SiO₂ monolith comprising cells with a dissolution rate from greater than or equal to 2 or 4 percent wherein the biological agent is a cell or protein (instant claims 21, 27, 29, 33 to 35, 39, and 46 to 47). The '643 application claims a silica sol fiber with a solubility rate of 0.2 to 20 weight percent per hour in simulated body fluid ('643, claims 24 and 30 to 33) which as evidenced by Kortesuo et al, 2001a provides a dissolution rate (as discussed *supra*). Further, the '643 application provides a composition further comprising a cell ('643, claim 25). This solubility in SBF is considered the bioresorption rate and as such make obvious instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Applicant's Arguments

Applicant has requested the provisional rejection be held in abeyance until one of the applications is allowed. Applicant's arguments are not considered persuasive as

'643 application has pending claims which anticipate the claims in the instant application.

NEW GROUNDS OF REJECTION NECESSITATED BY AMENDMENT

Claim Rejections – 35 USC § 112 Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

In light of applicant's 02/17/2010 response and claim amendments, the language in the claims does not clearly and distinctly delineate the claimed subject matter.

○ Claims 21, 27, 29, 33 to 35, 39, and 46 to 47 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. First, claims 20 and 28 recite a very fast bioabsorption rate but does not designate the metes and bounds for a very fast bioabsorption rate wherein claim 21 depends from claim 20 and claim 29 depends from claim 28. Second, claim 20 (page 3, line 7), claim 28 (page 14, line 4), and claim 38 (page 22, line10), upon which claims 21, 29, and 39 depend respectively, refers to changes which have not been addressed by this point in the claims and thus one needs to refer to a later portion of claim 20, 28, or 38 to determine what "changes" are required. Third, segment "a" of the claims 20 and 28 recite starting conditions but loosely refers to a process which makes the product and does not clearly designate starting conditions required to provide a sol-gel derived SiO₂ monolith with a very fast bioabsorption rate. Fourth, claims 20, 28, and 38 each recite either "b)i) the sol is, without induced changes" or "b)ii) a change or changes of the sol composition are induced" and thus recites the sol-gel may be formed with or without induced changes" but the applicant argues the present application provides a "starting point, and defines the provisos released to having these changes reduce the dissolution rate". Thus the applicant's argument asserts what changes are required but claims the sol-gel derived SiO₂ monolith with a very fast bioabsorption rate may be made without induced

changes. In fact, while applicant argues criticality of the parameters for making the gel, claim 20 recites the sol-gel may be formed with or without changes, with an optionally additional component, and drying may be started and completely finished within 30 minutes or started within 30 minutes but not finished within 30 minutes. Further, item "2)i)" recites forced drying is not carried out. Fifth, the metes and bounds for changes in are not clear as items "1" and "2" of claims 20 and 28 recite "deviating" from starting values, "carrying out induced changes by the addition of a component or components", addition of optional components wherein the "changes affecting any of the values i) – iii) of a)". Thus the claims recite a broad deviation even from the "range of values" which appear to be only a starting value. Sixth, claims 20 and 28 recite "deviating the temperature" but the metes and bounds for "deviating" are not clear. Further, applicant recites correlating to a "desired biodegradability" but has not recited an appropriate range for "desired biodegradability". Seventh, the applicant has amended the claims to recite a higher range in instant claim 27 (i.e. limited the dissolution rate ≥ 4 wt-%/h) but as claimed no parameter ranges have been changed to indicate such a change in starting parameters is crucial. Further, claims 34 and 47 recite the dissolution rate is ≥ 2 wt-%/h using the same parameters. Thus, the metes and bounds for the parameters which designate certain bioabsorption or dissolution rates are unclear and further, the extent or deviation of changes are unclear. Eighth, while the biologically active agent is recited as an optional component claim 20 recites "no biologically active agent other than SiO_2 itself" and claims 21, 29, and 39 recite "further comprising at least one biologically active agent other than SiO_2 itself" and thus the metes and bounds of what is comprised in a sol-gel derived SiO_2 monolith is unclear. Lastly, claims 20 and 28 recite "changes to the method correlating with the desired biodegradability" but the metes and bounds of changes, correlating, and desired biodegradability are unclear and thus considered indefinite. Thus the metes and bounds of these claims are unclear and as such claims 21, 27, 33 to 35, 39, and 46 to 47 are considered indefinite.

Conclusion

All claims are rejected; no claims are allowed.

THIS ACTION IS MADE FINAL AS NECESSITATED BY AMENDMENT.

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RAYMOND P. YEAGER whose telephone number is (571) 270-7681. The examiner can normally be reached on Mon - Thurs 8:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

R.P.Y.

/Leon B Lankford/
Primary Examiner, Art Unit 1651